AUTOLOGOUS NEUTRALIZATION OF HIV RESERVOIR OUTGROWTH IS STABLE OVER TIME DURING ART

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BACKGROUND

- We have previously demonstrated that individuals harbor variable proportions of autologous neutralization sensitive viral variants in their reservoir[1]. Variants that are resistant to autologous neutralization are thought to be most likely to rebound following analytical treatment interruption.
- **Question:** Is suppression of viral outgrowth mediated by autologous neutralizing antibodies (anAb) maintained in people living with HIV (PLWH) over time?
- **Implication:** A change in the proportion of anAb-resistant viruses in the latent reservoir could impact the timing and identity of viral rebound. An understanding of virus most likely to contribute to viral rebound is vital to developing clinical strategies to cure HIV.

METHODS

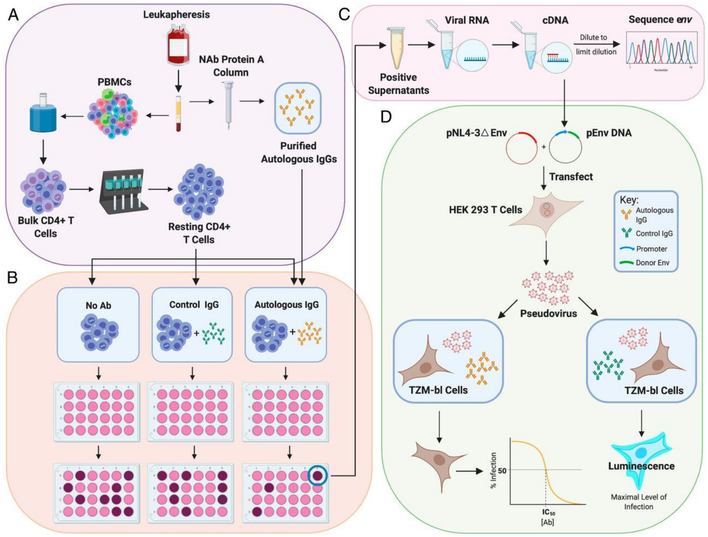

Fig. 1. **Evaluation of suppression of viral outgrowth by autologous neutralizing antibodies. (A)** Sample collection and processing **(B)** Modified QVOA set-up **(C)** Viral *env* gene sequencing and phylogenetic analysis **(D)** Experimental neutralization assay protocol

ADDITIONAL KEY INFORMATION

We would like to acknowledge the study participants and funding resources that have made this work possible.

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References:

[1] Bertagnolli LN, Varriale J, Sweet S, et al. Autologous IgG antibodies block outgrowth of a substantial but variable fraction of viruses in the latent reservoir for HIV-1. Proceedings of the National Academy of Sciences - PNAS. 2020;117(50):32066-32077.

aNAb-mediated suppression of outgrowth, and ***direct neutralization*** of reservoir isolates, are stable over time in individuals suppressed on ART

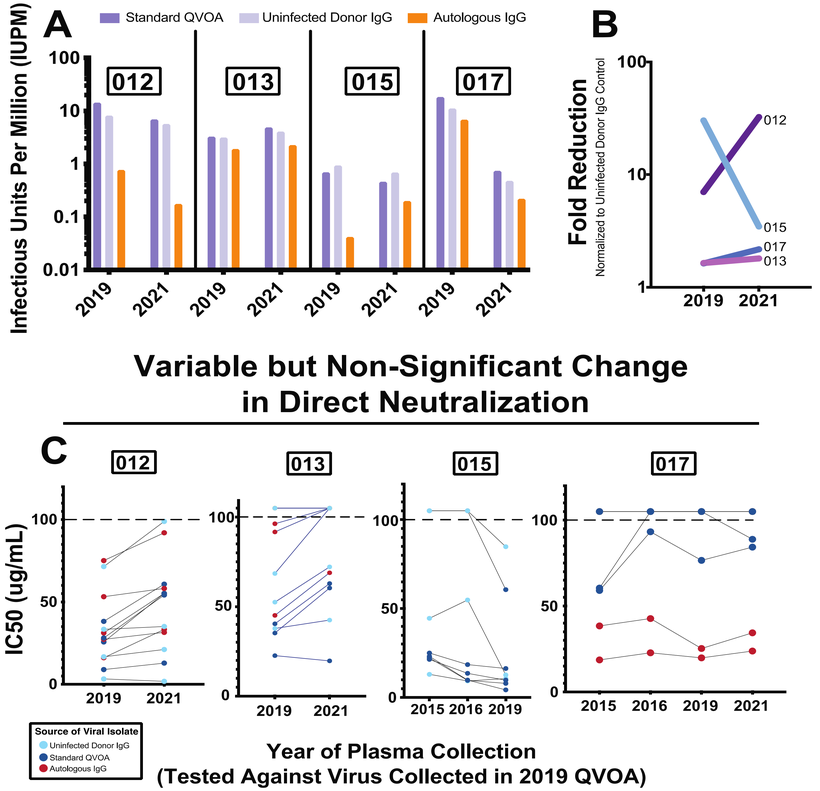
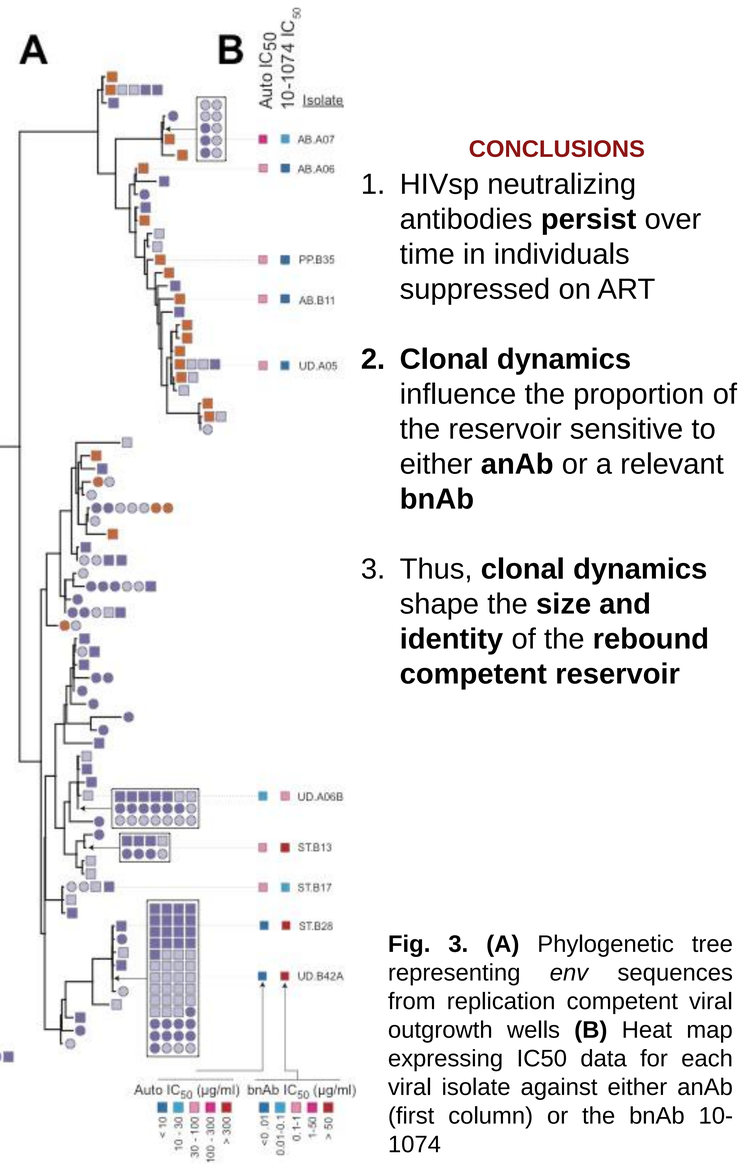


Fig. 2. (A) Decrease in IUPM represented in both timepoints across four individuals **(B)** Fold reduction in IUPM for four individuals across 2 timepoints. **(C)** IC50 of individual viral isolates from 2019 QVOA across plasma time points spanning 2-6 years

CONCLUSIONS

Adaptive Immunity plays an important role in preventing viral rebound from the reservoir.

- Suppression of viral outgrowth mediated by anAbs is maintained in follow-up sampling 2+ years after initial measurement
- In one patient (012), suppression was enhanced in the follow-up timepoint, suggesting an increase in the proportion of anAb sensitive variants in the latent reservoir



CONCLUSIONS

1. HIVsp neutralizing antibodies **persist** over time in individuals suppressed on ART
2. **Clonal dynamics** influence the proportion of the reservoir sensitive to either **anAb** or a relevant **bnAb**
3. Thus, **clonal dynamics** shape the **size and identity** of the **rebound competent reservoir**

Fig. 3. (A) Phylogenetic tree representing *env* sequences from replication competent viral outgrowth wells **(B)** Heat map expressing IC50 data for each viral isolate against either anAb (first column) or the bnAb 10-1074